REMARKS

This amendment is submitted in response to the Official Action mailed December 12, 2006. In view of the above claim amendments and the following remarks, reconsideration by the Examiner and allowance of the application is respectfully requested.

Claims 35, 37– 39 and 41 have been amended to more particularly point out and distinctly claim the subject matter applicants regard as the invention. In particular, Claim 35 has been amended to clarify that method is for inhibiting Factor Xa thrombin generation in a patient in need thereof, disclosed in the specification at page 171, lines 4 – 7 and page 173, lines 11-13. Claim 35 has also been amended to replace "heteroalkyl" with "heteroaralkyl" in the definition of R_{11}. This is disclosed in the specification at page 22, line 10. The structure of Claim 35 has been amended to clarify that X_{5a}, X_{5b} and X_{5c} may be positioned anywhere on the pyrrolopyridine ring, which is disclosed throughout the specification. Claim 35 has also been amended to clarify that when Y^1 and Y^2 form a heterocyclyl with the nitrogen atom to which they are attached, at least one carbon atom of the ring system is replaced with an atom other than carbon. This is disclosed in the specification at page 6, lines 9– 10. Finally, several self-evident typographical errors were also corrected. The same amendments have been made to Claim 39. None of the foregoing changes introduces new matter.

In addition, Claims 37 and 41 have been amended to delete the term "prodrug," which does not introduce new matter. Finally, claim 38 has been amended to replace "hirudin derivatives and analogs thereof with "hirudin" and "hirulogs." Hirulogs are disclosed in the specification at page 173, line 4, and also does not introduce new matter.

To be complete, new claim 43 has been added, directed to methods in which the patient is in need of treatment of a thromboembolism or a thrombotic occlusion. This is disclosed in the specification at page 1, lines 29 – 30 and also does not introduce new matter.

In view of the above claim amendments and new claim, the within application is believed to be in condition for allowance. Reconsideration of the rejections made by the Examiner is therefore respectfully requested.

Turning to the Official Action, claims 35-41 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim

the subject matter that applicant regards as the invention. The Examiner considered the language "condition of the arterial or venous vasculature" in Claim 35 to be indefinite because defining a disease by its underlying cause renders the scope of intended uses may read on diseases not yet known to be caused by or affected by such action. The Examiner considered the positions of X_{5a}, X_{5b} and X_{5c} in the structure of Claim 35 to be inconsistent with the requirement of Claim 35 that one of the X's be on the pyrrolo ring. The Examiner considered the term "heteroalkyl" in Claim 35 to be indefinite because the specification did not define such a term and in was unclear whether the group bonded to the pyrrolopyridine ring via a heteroatom or a carbon atom.

The Examiner considered the scope of Y^1 and Y^2 forming a heterocyclyl in Claim 35 to be indefinite because it was not clear whether the nitrogen atom to which they are attached is the only heteroatom. The Examiner considered the term "prodrug" to be unclear in Claim 37 and to lack antecedent basis in Claim 35 or Claim 36. The Examiner objected to Claim 41 for the same reason in the context of Claim 39 and 40. Finally, the Examiner considered the term "hirudin derivatives and analogs thereof" to be indefinite because the specification does not define what these compounds are." This rejection is respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

Claim 35 has been amended to clarify that the claimed method inhibits Factor Xa thrombin generation in a patient in need thereof. The conditions intended for treatment are readily identified by one having ordinary skill in the art. The diseases intended for treatment by the method of claim 35 are now clear. By amending claim 35 in this manner, this portion of the rejection of claims 35-38 as indefinite under 35 U.S.C. § 112, second paragraph has been traversed.

The structure of Claim 35 has been amended, as well as the structure of Claim 39, to clarify that X_{5a}, X_{5b} and X_{5c} may be positioned any-where on the pyrrolopyridine ring, which is consistent with the requirement that at least one X must be on the pyrrolo ring. By amending Claims 35 and 39 in this manner, this portion of the rejection of claims 35-41 as indefinite under 35 U.S.C. § 112, second paragraph has also been traversed.

Claim 35 has also been amended (as well as Claim 39) to clarify that when Y^1 and Y^2 form a heterocyclyl with the nitrogen atom to which they are attached, at least one carbon

atom of the ring system is replaced with an atom other than carbon. This clarifies whether additional heteroatoms may be present, so that amending claims 35 and 39 in this manner, traverses this portion of the rejection of claims 35-41 as indefinite under 35 U.S.C. § 112, second paragraph.

Finally, Claims 35 and 39 have been amended to replace "heteroalkyl" with "hetero-aralkyl," for which support exists in the specification. By amending Claims 35 and 39 to correct this typographical error, this portion of the rejection of claims 35-41 as indefinite under 35 U.S.C. § 112, second paragraph has also been traversed.

Turning to Claims 37 and 41, both claims have been amended to delete the term "prodrug" objected to by the Examiner. By amending claims 37 and 41 in this manner, this portion of the rejection of claims 35 – 41 as indefinite under 35 U.S.C. § 112, second paragraph has also been traversed.

Finally, Claim 38 has been amended to replace "hirudin derivatives and analogs thereof with "hirudin" and "hirulogs," compounds that are well-known and readily identified by those of ordinary skill in the art. By amending Claim 38 in this manner this portion of the rejection of Claims 35 – 41 as indefinite under 35 U.S.C. §112, second paragraph has been traversed.

By amending claims 35, 37-39 and 41 to clarify the conditions being treated, the positioning of the X groups on the pyrrolopyridine ring, the meaning of the term "hirudin derivatives and analogs thereof," the optional presence of additional heteroatoms on the heterocyclyl ring formed by Y^1 and Y^2 and that an N-heteroaralkyl rather than an N-hetero-alkyl is attached to A_4, and to delete the term "prodrug," this rejection of claims 35-41 as indefinite under 35 U.S.C. § 112, second paragraph has been overcome. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Next, claims 35-41 were rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. In particular, the Examiner considered the recited combinations of compounds for treating disease related to venous and arterial vasculature to render Claims 35, 39 and the claims depending therefrom "unduly broad." The Examiner also considered the specification to be non-enabling for pyrrolopyridine treatment methods

because no IC_{50} data was provided for any of the claimed compounds, especially given that pyrrolopyridines were not known inhibitors of Factor Xa and a large number of compounds were claimed. The Examiner considered it significant that the only compound actually tested was an isoquinoline. The Examiner also considered the specification to be non-enabling for both making and using compounds in which the pyrrolidinone ring is substituted with groups other than amino or amide groups. Finally, the Examiner also considered the specification to be non-enabling for pyrrolopyridine treatment methods because of the extensive research required to evaluate each and every compound within the cope of the independent claims and there is no guidance regarding of to make or obtain the multi-substituted compounds taught by the specification as being starting material for the claimed subject matter. This rejection is respectfully traversed in view of the above claim amendments for the following reasons.

The breadth of the independent claims are now limited to a scope for which adequate direction and guidance is presented in the specification in view of the state of the art related to Factor Xa inhibitors and the more precisely defined treatment objective, inhibition of Factor Xa thrombin generation. As was previously stated, regardless of the activity other pyrrollopyridine compounds have, the pyrrolidinone-pyrrolopyridine molecular core identified by the Examiner is reported by Applicant to have Factor Xa inhibiting activity. If one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, such as isoquinolines, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be sufficient to satisfy 35 U.S.C. § 112, first paragraph. (See MPEP §2164.01(c)).

Enablement is thus not evaluated relative to compounds with similar structures, it is evaluated relative to compounds with similar activity. For inhibiting Factor Xa thrombin generation, undue experimentation is not required for one of ordinary skill in the art guided by the present specification to apply the presently claimed pharmaceutical composition to the presently claimed treatment method by comparison of the inhibitory activities of the inventive compositions to other known Factor Xa inhibitor compositions.

Further, the large number of embodiments in general or ring substituent groups in particular, is not dispositive of enablement. The standard is not whether undue experimentation is required to make and use every compound within the scope of the claim, the standard is whether undue experimentation is required to make any compound within the scope of a

claim. Claim breadth alone is not tantamount to undue experimentation and non-enablement. A rejection of the claims as broader than the enabling disclosure is generally not appropriate when one skilled in the art can readily determine any one of the claimed embodiments. *Amgen v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), *cert. denied*, 502 U.S. 856 (1991). *See also,* M.P.E.P §2164.08.

In the present situation, the making of each and every compound within the scope of the claims is a matter of routine chemistry in view of the guidance provided by the present specification. The specification also provides adequate guidance for determining the appropriate dosage for each compound, particularly in view of the more precisely defined treatment objective. Amended Claim 35 is directed to treatment methods adequately enabled by the teach-ings of the specification viewed in the context of the state of the art for inhibiting Factor Xa thrombin generation. In view of the Factor Xa state of the art, amended pharmaceutical composition claim 39 is adequately enabled as well.

Claims 35-41 therefore satisfy the enablement requirements of 35 U.S.C. §112, first paragraph as it relates to compositions inhibiting Factor Xa thrombin generation and treat-ment methods. By amending claim 35 so that it is now directed to a method for inhibiting Factor Xa thrombin generation in a patient in need thereof, and similarly amending claim 39, this rejection of claim 35-41 for lack of enablement under 35 U.S.C. §112, first paragraph has thus been overcome. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

In view of the above claim amendments and the foregoing remarks this application is now in condition for allowance. Reconsideration is respectfully requested. The Examiner is requested to call the undersigned at the telephone number indicated below if there any issues remaining in this application to be resolved. Finally, if there are any additional charges in connection with this response, the Examiner is authorized to charge Applicants' Deposit Account No. 19-5425 therefor.

Respectfully submitted,

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